## REMARKS

New claims 23-27 have been added. Support for the new claims can be found in original claims 9-13 and in the specification, for example, at page 2, lines 1-5. With these amendments, claims 9-13 and 23-27 are pending in the application. No new matter has been added by these amendments.

Rejection Under 35 U.S.C. § 103

Claims 9-13 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent 6,228,398 ("the '398 patent") in combination with U.S. Patent 4,559,332 ("the '332 patent") and further in combination with U.S. Patent 5,160,744 ("the '744 patent") and as being unpatentable over U.S. Patent 6,596,456 ("the '456 patent") in combination with the '332 patent and further in combination with the '744 patent. Applicants respectfully disagree with the claim rejections and respectfully submit that the Office is improperly engaging in hindsight reconstruction based on Applicants' disclosure.

The Federal Circuit has repeatedly noted: "it is impermissible to use the claimed invention as an instruction manual or 'template' to piece together the teachings of the prior art so that the claimed invention is rendered obvious. This court has previously stated that '[o]ne cannot use hindsight reconstruction to pick and choose among isolated

disclosures in the prior art to deprecate the claimed invention.'" *In re Fritch*, 23 USPQ2d 1780, 1784 (Fed. Cir. 1992), citing *In re Fine*, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988); *see also In re Gorman*, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991). The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination and there must be a suggestion or motivation in the reference to do so. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990); (MPEP 2143.01). There is no suggestion or motivation in the cited references to combine the references in the manner suggested by the Office.

The '398 patent relates to a multiparticulate modified release composition that includes an immediate release component and a modified release component. The Office points out that the reference does not teach "that the anti-hypertensive agent is an aldosterone antagonist or release of the active agent in accordance with the diurnal cycle of plasma aldosterone concentration." See Office Action, page 3, ¶ 6.

The '456 patent relates to an osmotic device that is said to provide a controlled release of diltiazem and a rapid release of an ACE inhibitor diuretic compound. See the '456 patent, col. 1, lines 12-15. As noted by the Office, the reference does not disclose an aldosterone antagonist or release of a drug in

accordance with the diurnal cycle of plasma aldosterone concentration. See Office Action, page 3, ¶ 6.

The '332 patent describes spiroxane compounds that are said to have aldosterone-antagonist action and to be useful in the treatment of conditions such as hypertension. The '332 patent, col. 3, lines 38-47. As noted by the Office, the reference does not disclose the combination of aldosterone antagonists with a second formulation containing a second anti-hypertensive agent. See Office Action, page 3, ¶ 7. In addition, the reference says nothing about releasing the drug in accordance with the diurnal cycle of plasma aldosterone concentration in a subject.

The '744 patent relates to dosage forms for providing delayed delivery of a drug. The '744 patent, abstract. In an example, the reference describes controlled delivery of verapamil whereby the drug is released to coincide with the early morning rise of blood pressure, which is associated with hypertension and angina. Id. at col. 12, lines 29-34.

Applicants respectfully submit that the references lack the suggestion or motivation to combine that is necessary to support an obviousness rejection. The Office's contention that one skilled in the art would combine either of the '398 patent or the '456 patent with the '332 and '744 patents is based on improper hindsight reconstruction. The references do not discuss or suggest the desirability of providing a composition

containing a delayed release formulation of an aldosterone antagonist that provides a drug concentration corresponding to the diurnal cycle of plasma aldosterone concentration. Indeed, the references do not even mention or contemplate the diurnal cycle of plasma aldosterone concentration. The references, therefore, do not support a § 103(a) rejection of claims 9-13. Withdrawal of the rejection of these claims is respectfully requested.

Allowability of New Claims 23-27

New claims 23-27 are independently allowable. None of the references cited by the Office teach or suggest the invention as claimed in claims 23-27, including the limitation that the aldosterone antagonist is selected from eplerenone or spironolactone. Claims 23-27 are therefore believed to be allowable.

Should the Examiner believe a discussion of this matter would be helpful, he is invited to telephone the undersigned at (312) 913-0001.

Respectfully submitted,

Date: September 4, 2003 By: Raafat Shaltout

Raafat Shaltout
Reg. No. 45,092

McDonnell Boehnen Hulbert & Berghoff
300 South Wacker Drive
Chicago, IL 60606
Telephone: (312) 913-0001